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(54) **METHODS FOR TREATING POST-TRAUMATIC STRESS DISORDER**

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(58) **Field of Classification Search**

None

See application file for complete search history.

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(57) **ABSTRACT**

Embodiments herein relate to nutritional supplements for treating post-traumatic stress disorder in human beings, and to methods of using the same. In particular examples, the nutritional supplement comprises an amino acid secretagogue composition.

16 Claims, 2 Drawing Sheets

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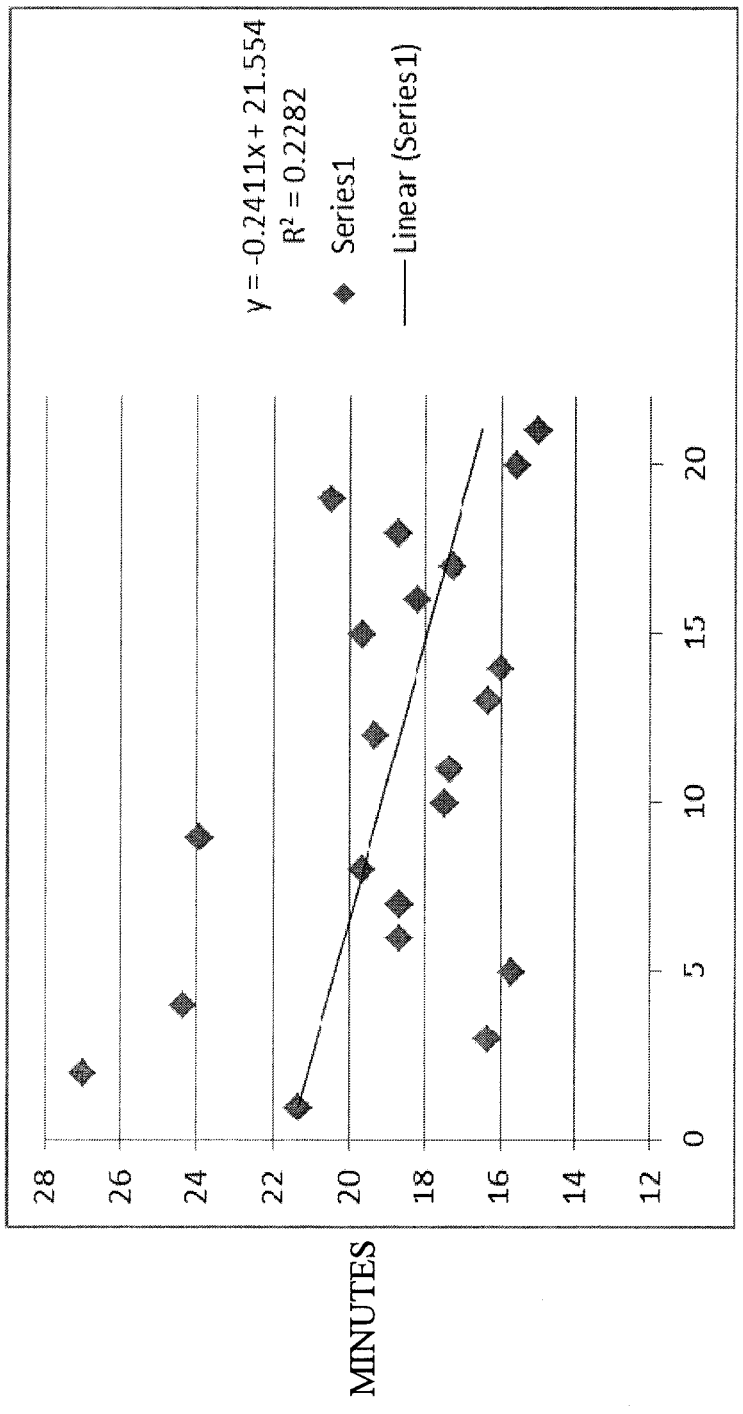

Figure 1: Time to fall asleep

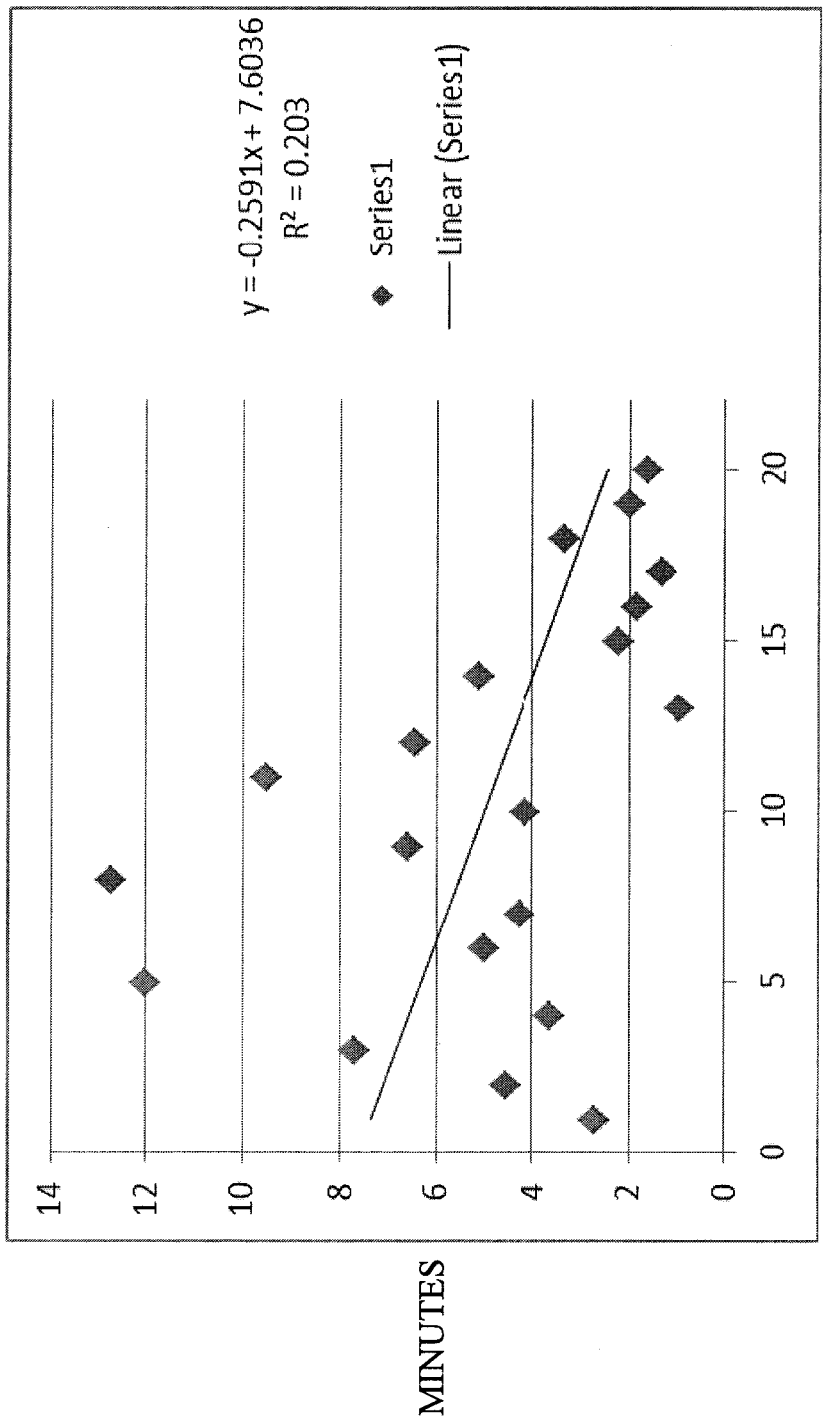

Figure 2: Time awake during sleep

METHODS FOR TREATING POST-TRAUMATIC STRESS DISORDER

TECHNICAL FIELD

Embodiments of the invention generally relate to methods and supplements for treating post-traumatic stress disorder.

BACKGROUND

Posttraumatic stress disorder (PTSD) is a severe anxiety disorder that can develop after exposure to any event that results in psychological trauma. This event may involve the threat of death to oneself or to someone else, typically overwhelming the individual's ability to cope. As an effect of psychological trauma, PTSD is less frequent and more enduring than the more commonly seen acute stress response. Diagnostic symptoms for PTSD include re-experiencing the original trauma(s) through flashbacks or nightmares, avoidance of stimuli associated with the trauma, and increased arousal—such as difficulty falling or staying asleep, anger, and hypervigilance.

Posttraumatic stress disorder is classified as an anxiety disorder, characterized by aversive anxiety-related experiences, behaviors, and physiological responses that develop after exposure to a psychologically traumatic event (sometimes months after). Its features persist for longer than 30 days, which distinguishes it from the briefer acute stress disorder. These persisting posttraumatic stress symptoms cause significant disruptions of one or more important areas of life function.

Although most people (50-90%) encounter trauma over a lifetime, only about 8% develop full PTSD. Vulnerability to PTSD is believed to stem from an interaction of biological diathesis, early childhood developmental experiences, and trauma severity.

A variety of medications has shown adjunctive benefit in reducing PTSD symptoms, but there is no clear drug treatment for PTSD. Positive symptoms (re-experiencing, hypervigilance, increased arousal) generally respond better to medication than negative symptoms (avoidance, withdrawal), and it is recommended that any drug trial last for at least 6-8 weeks.

Medication classes that have been used for symptom management include: SSRIs (selective serotonin reuptake inhibitors, such as citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine, and sertraline); anti-depressants (such as, bupropion, venlafaxine, sertraline, fluoxetine, nefazodone, heterocyclics, and paroxetine); alpha-adrenergic antagonists (such as prazosin and clonidine); anti-convulsants, mood stabilizers, anti-aggression agents (such as carbamazepine, zolpidem, lamotrigine, valproic acid, and buspirone); antipsychotics; atypical antidepressants (such as nefazodone and trazodone); beta blockers; benzodiazepines; glucocorticoids; heterocyclic/tricyclic anti-depressants (such as amitriptyline and imipramine); and monoamine-oxidase inhibitors (MAOIs). Medication classes that have been used for symptom prevention include: alpha-adrenergic antagonists; beta blockers; and glucocorticoids.

A direct correlation has been observed between low growth hormone curves at onset of sleep and sleep problems in PTSD. (See, e.g., van Liempt, Decreased nocturnal growth hormone secretion and sleep fragmentation in combat-related posttraumatic stress disorder; potential predictors of impaired memory consolidation, Psychoneuroendocrinology (2011) 36, 1361-1369).

It would be desirable to provide a nutritional supplement for treating post-traumatic stress disorder.

BRIEF SUMMARY OF THE INVENTION

Described herein are nutritional supplement and method of using the same. The nutritional supplement includes an amino acid secretagogue composition, which, taken orally, stimulates the pituitary gland to release hGH.

Some embodiments include an oral nutritional supplement that comprises L-arginine, oxo-proline, and L-lysine.

A particular embodiment of the present disclosure relates to an oral nutritional supplement that includes the amino acids l-lysine, l-arginine, oxo-proline, and one of either cysteine or glutamine. The amino acids may be delivered as non-toxic salts thereof, effective complexes thereof, stable chelates thereof, active esters thereof, functional derivatives thereof, and mixtures thereof which are effective to increase hGH levels in the general population.

Another particular embodiment relates to an oral nutritional supplement that consists essentially of l-lysine HCl, l-arginine HCl, oxo-proline, N-acetyl-l-cysteine, l-glutamine, and schizonepeta (aerial parts) powder.

Other embodiments are drawn to methods of treating post-traumatic stress disorder in humans that include orally administering the disclosed nutritional supplement to a human being suffering from post-traumatic stress disorder.

BRIEF DESCRIPTION OF THE FIGURES

FIG. **1** shows a linear regression analysis of time to fall asleep with continued use of the supplement over time; and

FIG. **2** shows time awake during sleep over time with continued use of the supplement.

DETAILED DESCRIPTION OF THE INVENTION

The present invention relates to a nutritional supplement for use by a human being. The present invention is drawn to a nutritional supplement and method of using the same. The nutritional supplement is an amino acid secretagogue composition, which, taken orally, treats one or more post-traumatic stress disorder (PTSD) symptoms. The supplement of the present invention works as a dietary supplement by assisting the body's own ability to treat PTSD symptoms naturally in a manner which is safe and effective, as well as being affordable.

A particular embodiment of the present disclosure relates to an oral nutritional supplement that includes l-lysine, l-arginine, oxo-proline, and one of either cysteine or glutamine. The supplement may additionally include both cysteine and glutamine and/or schizonepeta powder. In particular embodiments, a functional dosage includes the l-arginine at a level between 0.1-6 mmol and the oxo-proline between 0.1-8 mmol, and/or the l-lysine in an amount between 0.1-12 mmol. The cysteine and/or glutamine may be contained at a level between 0.001-6 mmol. In another particular embodiment, a functional dosage includes the l-arginine at a level between 2.5-4.5 mmol and the oxo-proline between 4-6 mmol, and/or the l-lysine in an amount between 7-9 mmol. The cysteine and/or glutamine may be contained at a level between 0.001-0.5 mmol. The cysteine can be n-acetyl L-cysteine and the glutamine may be l-glutamine. The amino acids may be delivered as non-toxic salts thereof, effective complexes thereof, stable chelates thereof, active esters thereof, functional derivatives thereof, and mixtures thereof which are effective to increase hGH levels in the general population. The nutri-

tional supplement may be present in an amount of 2.9 grams. The nutritional supplement may be in any acceptable and known oral formulation, such as powder, tablet, capsule, liquid, or wafer form.

Another particular embodiment relates to an oral nutritional supplement that consists essentially of l-lysine HCl, l-arginine HCl, oxo-proline, N-acetyl-l-cysteine, l-glutamine, and schizonepeta (aerial parts) powder. In particular embodiments, a functional dosage includes the l-arginine HCl at a level between 0.1-6 mmol and the oxo-proline between 0.1-8 mmol, and/or the l-lysine HCl in an amount between 0.1-12 mmol. The n-acetyl L-cysteine and/or l-glutamine may be contained at a level between 0.001-6 mmol. In another particular embodiment, a functional dosage includes the l-arginine HCl at a level between 2.5-4.5 mmol and the oxo-proline between 4-6 mmol, and/or the l-lysine HCl in an amount between 7-9 mmol. The n-acetyl L-cysteine and/or l-glutamine may be contained at a level between 0.001-0.5 mmol. The nutritional supplement may be in any acceptable and known oral formulation, such as powder, tablet, capsule, liquid, or wafer form.

Other embodiments are drawn to methods of increasing human growth hormone in humans that include orally administering the disclosed nutritional supplement to a healthy human being. As used herein, "healthy human being" means a human being without any physiological deficiency in hGH independent of age. Particular embodiments of the invention relate to oral administration of the disclosed nutritional supplement to a human that is at least 30 years old. The nutritional supplement may be administered from one to three times daily or, alternatively, may be administered every other day, or may be administered once a week. In particular embodiments, the nutritional supplement may be administered on an empty stomach.

In accordance with the "consist essentially of" and "consisting essentially of" language, the nutritional supplement of the third embodiments is essentially limited to the aforementioned ingredients and does not include any additional active ingredients intended to add nutritional content (e.g., vitamins, minerals, etc.), but may include additional ingredients not intended to add nutritional content such as ingredients intended to fulfill a non-nutritional purpose (e.g., coloring, fillers, flavoring, an ingredient for maintaining the structural form, etc.).

Each ingredient of the nutritional supplement of the present invention may be prepared in accordance with any method known to one of ordinary skill in the art. Alternatively, each ingredient may be obtained in a fully prepared from a commercially available source.

The nutritional supplement of the present invention may be in any suitable oral administration form, including but not limited to: a chewable form, a liquid form, a spray form, a capsule form, a suppository form, dissolvable wafer, and a powder form.

Irrespective of the structural form of the nutritional supplement, the ingredients of the nutritional supplement may be distributed homogeneously or non-homogeneously within the nutritional supplement.

The nutritional supplement of the present invention may be ingested on a regular basis, such as a daily or weekly intake at a dosage tailored to an individual's needs; i.e., the nutritional supplement is to be taken regularly as multiples (1×, 2×, etc.) of the structural units (pills, tablets, capsules, liquid dose, etc.) in accordance with the needs of the individual. For example, a senior citizen leading a sedentary life may need higher daily doses than does a young person engaged in regular strenuous exercise (e.g., a weight lifter). Alternatively, the nutritional supplement of the present invention may be ingested on an as-needed basis at a dosage tailored to the individual's needs. Medical or nutritional counseling may be beneficial for arriving at a desirable or optimal dosage tailored to the individual's needs.

The combination of types of amino acids, mass ranges, and specific formulations have been selected to be synergistically balanced and of adequate quantity to achieve the desired physiological effect, namely, treatment of PTSD symptoms. Improper combinations of the amino acids may be ineffective. The component amino acids are synergistic in the sense that several of them when combined together, synergistically treat one or more symptoms of PTSD. The combination was also chosen to reduce or inhibit chemical combination or reaction between the amino acids.

EXAMPLES

Example 1

A double-blind clinical study involved 15 healthy subjects [10 males, 5 females; mean age=33±7 years]. Each subject completed a baseline Epworth Sleepiness Scale self-report questionnaire and a standardized assay of usual sleep habits. All subjects were deemed to have average sleep parameters within a normal range.

The subjects were then provided a three week supply of a novel supplement SeroVital (2.9 g/dose blend of l-lysine HCl, l-arginine HCl, oxo-proline, N-acetyl-l-cysteine, l-glutamine, and schizonepeta (aerial parts) powder). The novel SeroVital blend has been shown previously to increase serum human growth hormone hGH levels by 8 times (equivalent to 682%) 120 minutes after a single dose in healthy male and female volunteers. Because night-time onset of hGH has been directly correlated to sleep efficiency, we investigated sleep patterns with continued use of the supplement when taken on an empty stomach, two hours after dinner prior to bedtime, every night for three weeks. On each trial day, subjects reported 1) time went to bed; 2) time of final wakening; 3) estimated time to fall asleep; 4) time of awakening during sleep/length of time awake. Data was compiled by day for estimated time to fall asleep and length of time awake during sleep in order to assess sleep efficiency. Daily values for each measure were plotted as an average (±S.D.) among the subjects over the time course of the study, and a linear regression was tabulated to assess overall trends over time. All available data was included in the analysis.

Linear regression analysis showed that both estimated time to fall asleep (FIG. **1**) and time awake during sleep (FIG. **2**) tended to decrease over time with continued use of the supplement over the time course of the study. Time to fall asleep decreased with an average slope of −0.24 min/day, and time awake during sleep decreased by an average slope of −0.26 min/day. Overall, these results so a trend towards greater sleep efficiency by measurements of both time to fall asleep and time awake during sleep, both with a quantified average decrease of about 0.25 min/day over three weeks with regular nighttime use of the novel SeroVital supplement (when taken as directed, on an empty stomach, two hours after dinner prior to bedtime).

Example 2

Veterans with PTSD are recruited through outpatient clinics and Veteran Affairs Medical Centers. Trauma controls (TC; veterans without PTSD) and healthy controls (HC; service members never deployed or civilians) are recruited

through advertisements. Controls are matched with the PTSD group for age, year of deployment (TC), and region of deployment (TC). All participants are screened for psychiatric illness. The diagnosis of PTSD is confirmed by the Clinician Administered PTSD Scale (CAPS) and patients are included when a score of over 50 is obtained and there is an absence of psychiatric disorders other than mood and anxiety disorder. TCs are included when they meet the criteria for PTSD (experienced, witness, or was confronted with an event involving actual or threatened death or serious injury to self or others), but has a CAPS score below 18. All participants are medically healthy individuals and are free from psychotropic medication and alcohol or drug dependence in the past six months. All control subjects are without without a history of psychiatric disorders and without sleep complaints.

Sleep registrations during two consecutive nights are conducted in a sleep laboratory. Sleep recordings are acquired, including bipolar derivations of EMG, EOG for vertical and horizontal eye movements, EEG, and ECG.

To assess declarative memory consolidation, a 15 word task is administered three hours before sleep on the second evening. Fifteen neutral one syllable words are visually presented on a computer screen, and repeated three times. Every presentation is followed by a free immediate recall and is assessed the next morning between 30-45 minutes after awakening.

Sleep data are analyzed in 30 second epochs by an experienced sleep technician who is blind to PTSD diagnosis. The number of spontaneous awakenings for Stage 2 sleep, slow wave sleep, or rapid eye movement sleep are determined for the first half of the night. Total sleep time is also determined.

While embodiments of the present invention have been described herein for purposes of illustration, many modifications and changes will become apparent to those skilled in the art. Accordingly, the appended claims are intended to encompass all such modifications and changes as fall within the true spirit and scope of this invention.

We claim:

1. A method of improving sleep and enhancing memory in a subject in need thereof, the method comprising:

orally administering a nutritional supplement composition in unit dosage form to the subject, wherein the unit dosage consists of:

0.1 to 6 mmol L-arginine;

0.1 to 8 mmol Oxo-proline;

0.1 to 12 mmol L-lysine;

0.001 to 6 mmol N-acetyl L-cysteine; and

0.001 to 6 mmol L-glutamine.

2. The method of claim **1**, wherein the L-arginine is L-arginine HCl salt, or L-lysine is L-lysine HCl salt, or both.

3. The method of claim **1**, wherein the unit dosage form has a mass of 2.9 grams.

4. The method of claim **1**, wherein the unit dosage form is a powder, tablet, capsule, liquid, or wafer.

5. The method of claim **1**, wherein the unit dosage form is administered to the subject from one to three times daily.

6. The method of claim **1**, wherein the unit dosage form is administered to the subject once a week.

7. The method of claim **1**, wherein the unit dosage form is administered to the subject on an empty stomach.

8. The method of claim **1**, wherein the subject is a female.

9. The method of claim **1**, wherein the subject exhibits one or more of: re-experiencing an original trauma through flashbacks or nightmares, avoidance of stimuli associated with an original trauma, increased arousal, difficulty falling or staying asleep, anger, and hypervigilance.

10. A method for improving sleep in a human subject in need thereof, the method comprising:

orally administering a nutritional supplement composition in unit dosage form to the human subject, wherein the unit dosage consists of:

0.1 to 6 mmol L-arginine;

0.1 to 8 mmol Oxo-proline;

0.1 to 12 mmol L-lysine;

0.001 to 6 N-acetyl L-cysteine;

0.001 to 6 L-glutamine; and

about 125 μg Schizonepeta aerial parts powder.

11. The method of claim **10**, wherein the nutritional supplement is provided in an amount of 2.9 grams.

12. The method of claim **10**, wherein the nutritional supplement is provided in powder, tablet, capsule, liquid, or wafer form.

13. The method of claim **10**, wherein the nutritional supplement is administered from one to three times daily.

14. The method of claim **10**, wherein the nutritional supplement is administered once a week.

15. The method of claim **10**, wherein the nutritional supplement is administered on an empty stomach.

16. The method of claim **10**, wherein the subject is female.

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